

## REMARKS

### I. Status of the Claims

Claims 1-11 are pending in the application.

Claims 1, 4-6, and 9-11 are amended.

Claims 12-15 are new.

### II. Amendments to the Claims

Claim 1 is amended to recite the process steps using present perfect verb tense, in accord with standard U.S. practice. Claim 1 is also amended to recite that the reacting occurs at -5 to -15°C. Support can be found, for example, in original claim 1 and in the third paragraph on page 3 of the specification as filed. Claim 1 is further amended to recite "wherein said fludarabine is not anhydrous." Support can be found, for example, in the first paragraph on page 3 of the specification as filed.

Claims 4-6 and 10-11 are amended for compliance with U.S. practice.

The subject matter of claims 4, 5, 6, and 10 are presented in new claims 12-15.

Claim 9 is amended to recite -10 to -15° C. Support can be found, for example, in the second paragraph of Example 1 on page 4 of the specification as filed.

Accordingly, the amendments to the claims do not introduce new subject matter.

### III. Rejections under 35 U.S.C. §112, second paragraph.

Claims 1, 9, and 11 were rejected under 35 U.S.C. 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, the Examiner noted that claims 1 and 9 recite "less than -5° C" and claim 11 recites "less than -10°

C." The Examiner thus alleges that claims 1, 9 and 11 are indefinite because no lower limit is recited.

Claim 1 is amended to recite -5 to -15° C and claims 9 and 11 are amended to recite -10 to -15° C.

Claims 4-6 and 10-11 were rejected under 35 U.S.C. 112, second paragraph as allegedly being indefinite for not clearly setting forth the metes and bounds of the patent protection desired. Specifically, the Examiner notes that claims 4-6 and 10-11 each recite a narrow limitation that falls within broad limitations recited in the same claim.

Applicants have amended claim 4-6 and 10-11 to remove the narrower limitation of each. Additionally, Applicants have added new claims 12, 13, 14, and 15 to recite the narrower limitation removed from claims 4, 5, 6 and 10, respectively.

Withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

#### IV. Rejections under 35 U.S.C. §103(a)

Claims 1-6 and 9-11 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Blumbergs et al. (WO 92/00312).

Claims 7-8 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Blumbergs et al. in view of Wikipedia (Solvent).

These rejections are respectfully traversed for the following reasons.

##### A. The Claimed Subject Matter

The present claims relate to a method to prepare fludarabine phosphate with a high yield and a high degree of purity without having to use anhydrous fludarabine.

##### B. The Cited Art

BLUMBERGS ET AL. describe a method to prepare fludarabine phosphate which comprises the use of anhydrous fludarabine (2-F-ara-A) . The starting fludarabine material must be vacuum-dried and the reactions carried out under essentially anhydrous conditions.

### C. Analysis

According to the M.P.E.P §2143, "to establish a prima facie case of obviousness, three basic criteria must be met." The third criterion is that "the prior art references (or references when combined) must teach or suggest all the claim limitations. Furthermore, "[i]f an independent claim is nonobvious under 35 U.S.C. §103 then any claim depending therefrom is nonobvious."

#### C1. Rejection of Claims 1-6 and 9-11 Based on Blumbergs et al.

Amended claim 1 recites a process for the preparation of fludarabine phosphate starting from fludarabine, wherein said fludarabine is not anhydrous.

Blumbergs et al. do not teach or suggest using non-anhydrous fludarabine as a starting material for the process of making fludarabine phosphate. In direct contrast to the claimed features of claim 1, Blumbergs et al. explicitly state (lines 33-35, page 2):

"It has been found that the 2-F-ara-A must be dried extensively under vacuum and that the reaction must be conducted under essentially anhydrous conditions."

A surprising aspect of the Applicants' claimed process is that by operating within the claimed temperature range, it is possible to obtain fludarabine phosphate having a high degree of purity even starting from a fludarabine material that is not anhydrous.

Because a skilled artisan would not have had a reasonable expectation of success in achieving the presently claimed methods, and because the references, alone or in combination, fail to teach all the limitations of the present claims, the

standard for obviousness has not been met. Applicants respectfully request withdrawal of the rejections under 35 U.S.C §103.

C2. Rejection of Claims 7-8 Based on Blumbergs et al. in view of Wikipedia

As noted above, amended claim 1 recites a process for the preparation of fludarabine phosphate starting from fludarabine, wherein said fludarabine is not anhydrous. Blumbergs et al. teach a method of preparing fludarabine phosphate starting from a fludarabine that is essentially anhydrous.

Claim 7 depends upon amended claim 1. Claim 8 depends upon claim 7. Therefore, claims 7-8, which directly or indirectly depend from claim 1, patentably define over the cited art for the same reason that claim 1 does. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

III. Conclusion

In view of the foregoing, the applicants submit that the claims pending are in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Respectfully submitted,  
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Date: 4/28/08

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